

RECEIVED

TECH CENTER 1600/2900



+ Dox

³⁵S-Metabolic Labeling

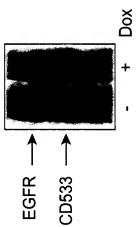
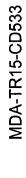
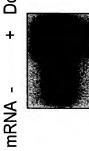


Figure 1B

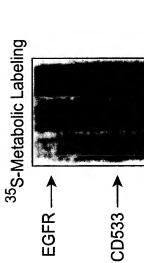




+ Dox

mRNA -

MCF-TR5-CD533



- + Lysate

Dox

Figure 1A

TRANSMITTAL OF FORM		Docket No. 02940139AA		
In Re Application Of: Schmidt-Ullrich, et al. APR 0 2 2003				
Serial No. 78 DEMARK 11/17/00	Confirmation No.	Examiner	Art Unit	
09/714,790 07/RADENM 11/17/00		Chen	1632	
Invention: GENETIC INHIBITION OF EPIDE CARCINOMA CELL RADIOSENSI	RMAL GROWTH F IZATION	ACTOR RECEPTOR AND		

· Marie



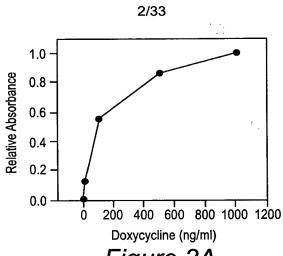
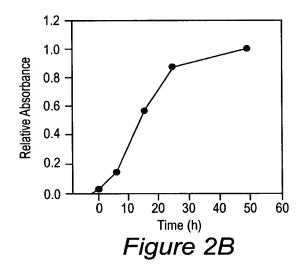


Figure 2A



1.2 1.0 – Output O.8 – O.0 – O 10 20 30 40 50 60 70 80 Time (h)

Figure 2C

TRANSMITTAL OF FO		Docket No. 02940139AA	
In Re Application Of: Schmidt-Ullrich, et a	il.		
Serial No. 11/17/00 Parish 11/17/00	Confirmation No.	Examiner Chen	Art Unit
Invention: GENETIC INHIBITION OF EL CARCINOMA CELL RADIOS	PIDERMAL GROWTH FA	CTOR RECEPTOR	R AND



3/33

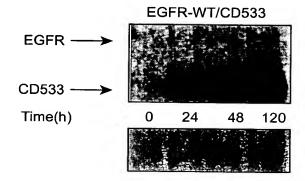
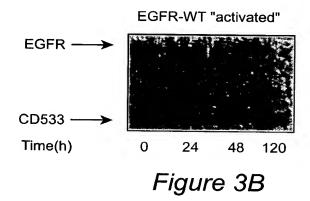


Figure 3A



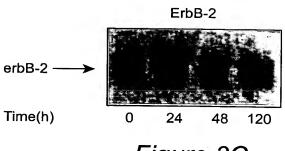


Figure 3C

TRANSMITTAL OF FORM		Docket No. 02940139AA	
In Re Application Of: Schmidt-Ullrich, et al. APR 0 2 2003		•	
Serial No. 11/17/00	Confirmation No.	Examiner	Art Unit _
09/714,790 TRADEW 11/17/00		Chen	1632
Invention: GENETIC INHIBITION OF EPIDER CARCINOMA CELL RADIOSENSI	RMAL GROWTH FAC ZATION	CTOR RECEPTOR A	AND

.

· Section of the sect

·



4/33

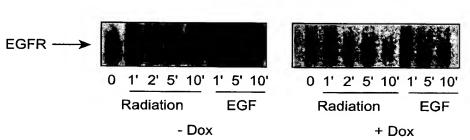


Figure 4A

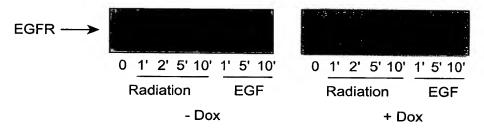
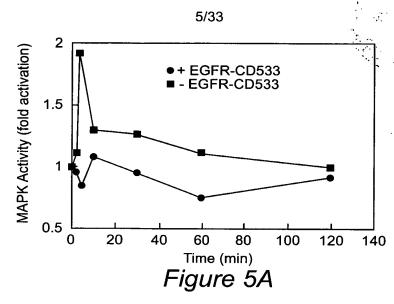
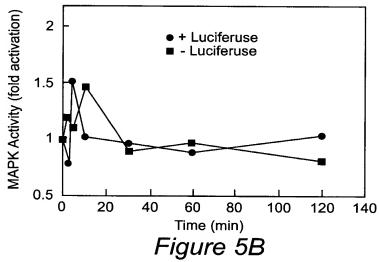


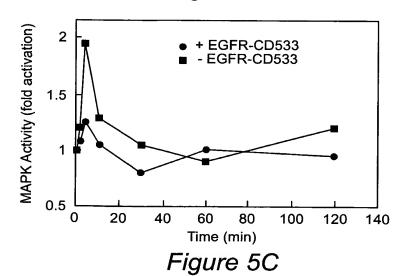
Figure 4B

TRANSMITTAL OF	Docket No. 02940139AA		
In Re Application Of: Schutta Ullrich, APR 0 2 2003	et al.		
Serial No.	Confirmation No.	Examiner	Art Unit
09/714,790 11/17/00		Chen	1632
Invention: GENETIC INHIBITION OF CARCINOMA CELL RADI	F EPIDERMAL GROWTH FAC	CTOR RECEPTOR A	ND









TRANSMITTAL OF FORMAL DRAWING	SS	Docket No. 02940139AA
In Re Application Of: Schmidt Ullrich, et al. APR 0 2 2003		
Serial No. Confirmation No.	Examiner	Art Unit
09/714,790 11/17/00	Chen	1632
Invention: GENETIC INHIBITION OF EPIDERMAL GROWTH CARCINOMA CELL RADIOSENSIZATION	H FACTOR RECEPTOR A	ND

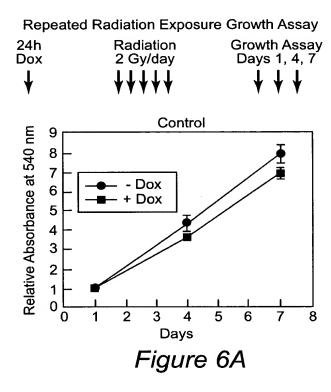
.

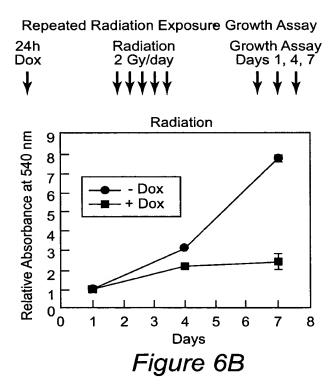
.

*



APR 0 4 2003





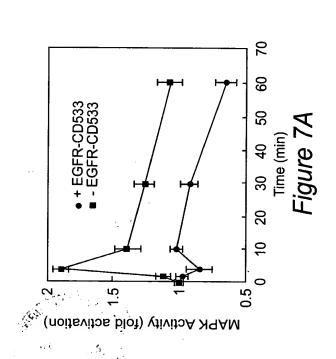
TRANSMITTAL OF FOR	RMAL DRAWINGS		Docket No. 02940139AA
In Re Application Of: Schmidt Ullrich, et al.			
Serial No. Filing Date 09/714,790 Filing Date 7RADEM 11/17/00	Confirmation No.	Examiner Chen	Art Unit 1632
Invention: GENETIC INHIBITION OF EPI CARCINOMA CELL RADIOSE	DERMAL GROWTH FAC	CTOR RECEPTOR A	ND

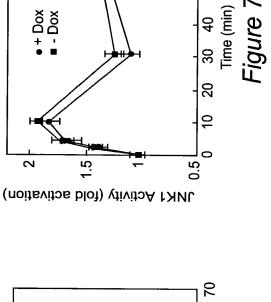
RECEIVED

APR 0 4 2003

TECH CENTER 1600/2900



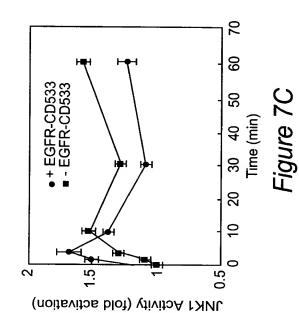


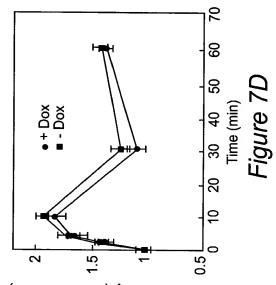


+ Dox

1.5

MAPK Activity (fold activation)





CARCINOMA CELL RADIOSENSIZATION Invention: GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND								
1632	Сћеп		00/L1/11	06L,41T/60				
 · jinU դĄ	Examiner	Confirmation No.	etsO gnilf	18in92 067,417\60				
			Schmidt-Ullrich, et al.	In Re Application Of:				
Docket No.		SENIWARD LOF FORMAL DRAWINGS						

<u>.</u>



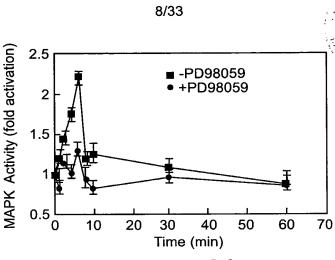
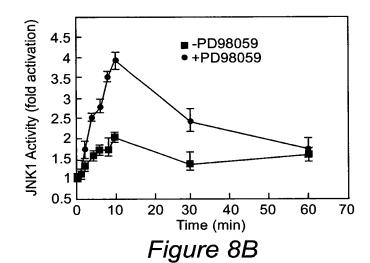


Figure 8A



JNK1 Activity (fold activation) 4.5 -EGFR-CD533, -PD98059 +EGFR-CD533, +PD98059 3.5 3 2.5 2 1.5 0.5 10 30 40 50 60 70 0 20 Time (min)

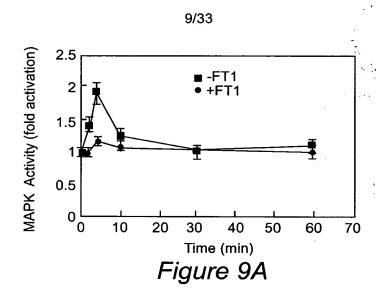
Figure 8C

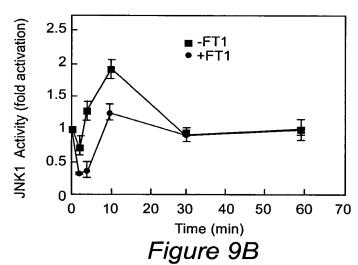
TRANSMITTAL OF FORMAL DRAWINGS			Docket No. 02940139AA		
In Re Application Of: Schmidt-Ullrich, et	al.				
Serial No. 1784 Enhig Date 09/714,790	Confirmation No.	Examiner	Art Unit		
		Chen	1632		
Invention: GENETIC INHIBITION OF E CARCINOMA CELL RADIO	PIDERMAL GROWTH FAC SENSIZATION	CTOR RECEPTO	R AND		

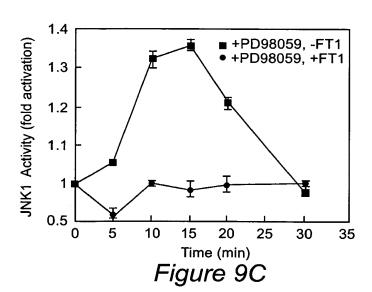
No.

:









TRANSM	ITTAL OF FO	RMAL DRAWINGS		Docket No. 92940139AA
APR 0 2 200	mid-Ullrich, et a	l		-
Serial No. 77 ADEMA	11/17/00	Confirmation No.	Examiner Chen	Art Unit
Invention: GENETIC INF CARCINOMA	IIBITION OF EI CELL RADIOS	PIDERMAL GROWTH FA ENSIZATION	CTOR RECEPTOR AND	
	75.			, • • •



10/33

			Со	ntro				F	PD9	805	9	*
Time (min)	0	2	4	10	30 60		0	2	4	10	30	60
c-Jun	× 5.			F-79-	he cint	ě	==;	=		نبد	3 74	
Relative c-Jun protein level	1	0.7	0.6	0.7	1.2 1.3		0.4	0.3	0.3	0.3	0.5	0.6

Figure 10A

c-Jun ^{P-Ser 63} →	SUL LOS COMPANY	Section Control
Relative c-Jun Ser 63 phosphorylation	1 0.4 0.6 5.6 17 3.9	0.4 1.2 4.8 12 16 6.6
Fold Alteration in c-Jun Ser 63 phosphorylation relative to c-Jun protein	1 0.6 7 8 14 3	1 3 16 41 32 11

Figure 10B

TRANSMITTAL OF FO		Docket No. 02940139AA	
In Re Application Of: Schmidt-Ullrich, et	al.		
Serial No. 11/17/00	Confirmation No.	Examiner	Art Unit
11/1//00		Chen	1632
Invention: GENETIC INHIBITION OF E CARCINOMA CELL RADIOS	PIDERMAL GROWTH FAC ENSIZATION	CTOR RECEPTOR A	ND ',

.

•

7



TECH CENTER 1600/2900 RECEIVED APR 0 4 2003

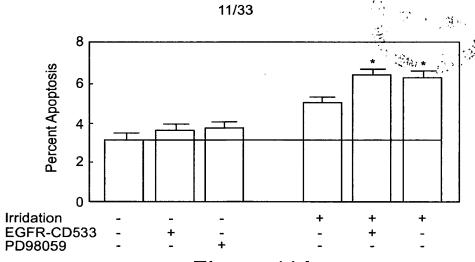
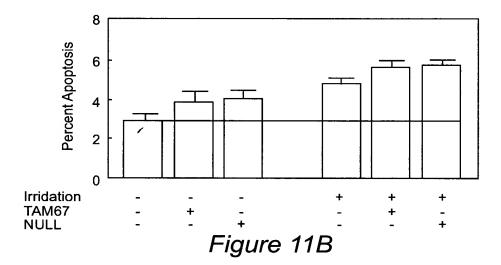
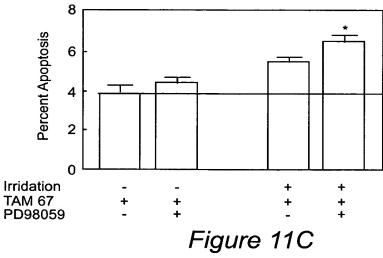


Figure 11A





TRANSMITTAL OF FORMAL DRAWINGS			Docket No. 02940139AA	
In Re Application of: Schmidt-Ullrich, et a	il.			
Serial No. Filipe Date	Confirmation No.	Examiner	Art Unit	1
09/714,790 A PADEMIN 1/17/00		Chen	1632	ye.
Invention: GENETIC INHIBITION OF EI CARCINOMA CELL RADIOS	PIDERMAL GROWTH F ENSIZATION	ACTOR RECEPTOR ANI		



12/33

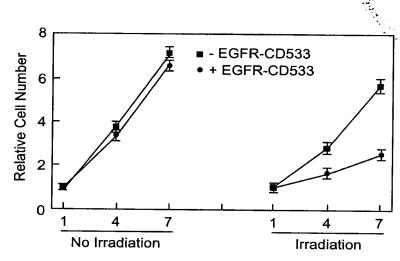


Figure 12A

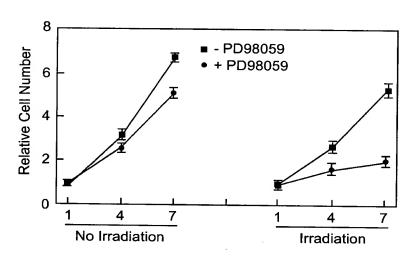


Figure 12B

TRANSMITTAL OF FORMAL DRAWINGS			Docket No. 02940139AA
In Re Application Of: Schmidt-Ullrich			
Serial No. Filing Date 09/714,790 A TRADEMARY 11/17/00	Confirmation No.	Examiner Chen	Art Unit 1632
Invention: GENETIC INHIBITION (CARCINOMA CELL RAI	OF EPIDERMAL GROWTH F DIOSENSIZATION	ACTOR RECEPTOR A	ND .

13/33

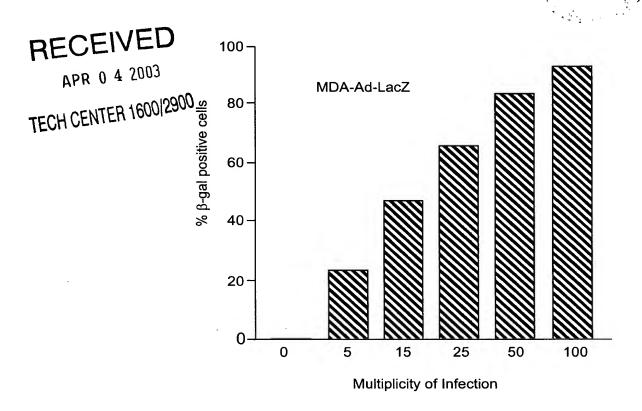


Figure 13

TRANSMITTAL OF FO	DRMAL DRAWINGS		Docket No. 02940139AA
In Re Application of Schmidt Ultrich, et a	al.		
Serial No. Filing Date	Confirmation No.	Examiner	Art Unit
09/714,790 RADENS 700		Chen	1632
Invention: GENETIC INHIBITION OF EXACTION A CELL RADIOS	PIDERMAL GROWTH FAC SENSIZATION	CTOR RECEPTOR AND	



14/33

RECEIVED

APR 0 4 2003

TECH CENTER 1600/2900

MDA-Ad-EGFR-CD533

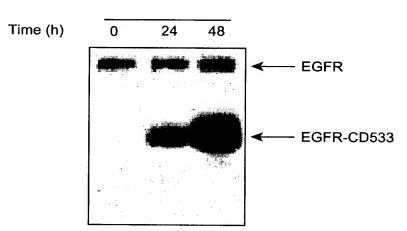


Figure 14

TRANSMITTAL OF FORMAL DRAWING	es	Docket No. 02940139AA
In Re Application Of: Schmidt-Ullrich, et al. APR 0 2 2003		
Serial No. Filing Date Confirmation No. 09/714,790 TRADEMIN 11/17/00	Examiner Chen	Art Unit
Invention: GENETIC INHIBITION OF EPIDERMAL GROWTH CARCINOMA CELL RADIOSENSIZATION	H FACTOR RECEPTOR	AND

The same

MDA-Ad-LacZ

2 Gy

Time (min)

EGFR Tyr-P →

MDA

5.0 2.5 2.3 2.1 15.2

Fold change 1 2.5 1.4 1.2

Figure 15B

Figure 15A

MDA-Ad-EGFR-CD533

15/33

1 1.1 0.8 0.8 1.0 4.1

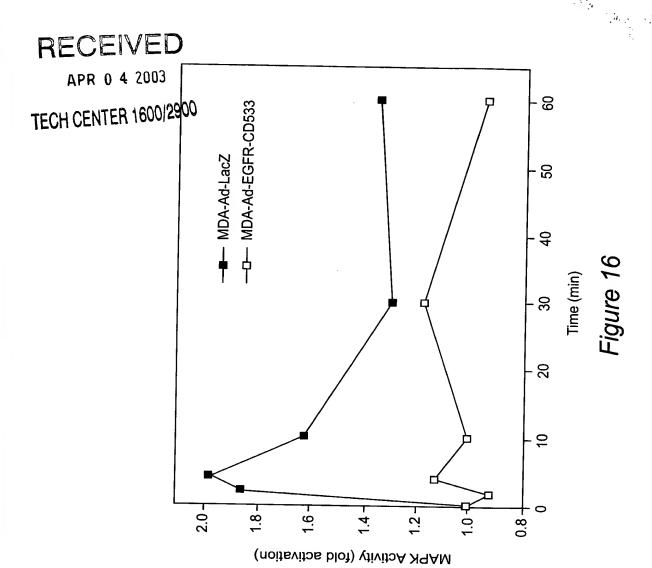
Figure 15C

ARN 12 TRINGENTS TRINGENTS

		DRMAL DRAWINGS		Docket No. 02940139AA
In Re Application Of:	Schmidt-Ullrich, et a	al.		
Serial No.	Fairing Date	Confirmation No.	Examiner Chen	Art Unit
Invention: GENETIC CARCING	INHIBITION OF E	PIDERMAL GROWTH FA	CTOR RECEPTOR ANI)

•

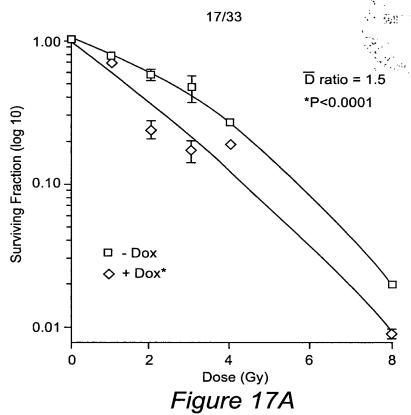


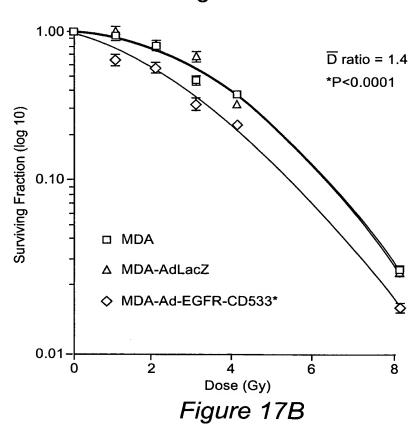


TRANSMITTAL OF FORMAL DRA	WINGS	Docket No. 02940139AA
In Re Application Of: Schmidt-Ullrich, et al. APR 0 2 2003 &		
Serial No. 7RAI EMARY 11/17/00 Confirmation 11/17/00	ion No. Examiner Chen	Art Unit 1632
Invention: GENETIC INHIBITION OF EPIDERMAL G CARCINOMA CELL RADIOSENSIZATION	ROWTH FACTOR RECEPTOR	RAND



APR 0 4 2003
TECH CENTER 1600/2900





				<u> </u>
TRANSMITTAL OF FORMAL DRAWINGS			Docket No. 02940139AA	
In Re Application Of:	Schmidt-Ullrich, et	al.		
Serial No.	Filing Date	Confirmation No.	Examiner	Art Unit
09/714,790	ADEMARY 11/17/00		Chen	1632
Invention: GENETIC CARCIN	C INHIBITION OF E OMA CELL RADIOS	PIDERMAL GROWTH FAC SENSIZATION	TOR RECEPTOR AND	
	*			·

·



RECEIVED

APR 0 4 2003

TECH CENTER 1600/2900

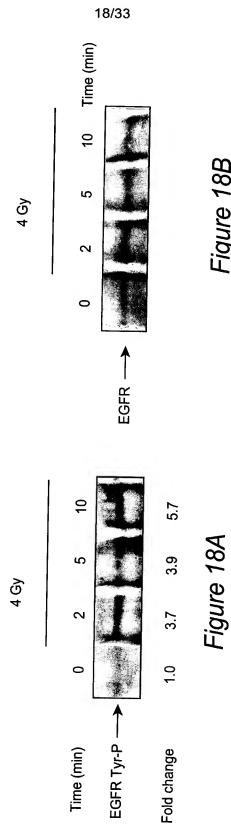


Figure 18B

In Re Application Of:

Serial No. Filing Date Confirmation No. Examiner Art Unit
09/714,790 11/17/00 Chen 1632

Invention: GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND CARCINOMA CELL RADIOSENSIZATION

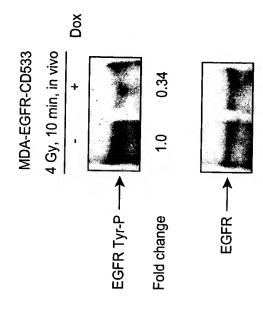
-



RECEIVED

APR 0 4 2003

TECH CENTER 1600/2900



ροχ

in vitro

in vivo

EGFR —

EGFR-CD533 —

MDA-EGFR-CD533

19/33

Figure 19A

Figure 19B

APR 0 2 2003 Docket No. TRANSMITTAL OF FORMAL DRAWINGS 02940139AA Schmidt-Ullrich, et al. In Re Application Of: Serial No. Filing Date Confirmation No. Examiner Art Unit 1632 09/714,790 11/17/00 Chen GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND CARCINOMA CELL RADIOSENSIZATION Invention:



RECEIVED

APR 0 4 2003

TECH CENTER 1600/2900

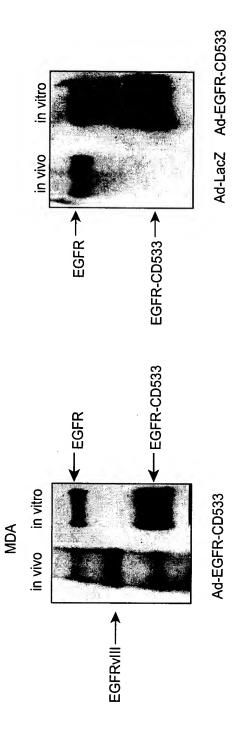


Figure 20A

Figure 20B

APR 0 2 7003				
TRADEMET TRA		ORMAL DRAWINGS		Docket No. 02940139AA
In Re Application Of	Schmidt-Ullrich, et	al.		
Serial No.	Filing Date	Confirmation No.	Examiner	Art Unit
				1

•

-

.



21/33

RECEIVED

APR 0 4 2003

TECH CENTER 1600/2900

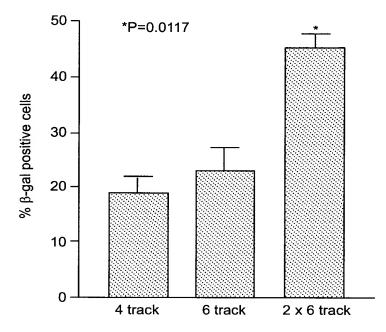


Figure 21

APR 0 2 2003 &				
		DRMAL DRAWINGS		Docket No. 02940139AA
In Re Application O	f: Schmidt-Ullrich, et a	al.		
Serial No.	Filing Date	Confirmation No.	Examiner	Art Unit
09/714,790	11/17/00		Chen	1632
Invention: GENET CARCI	IC INHIBITION OF EI NOMA CELL RADIOS	PIDERMAL GROWTH FA	CTOR RECEPTOR A	ND



22/33

RECEIVED

APR 0 4 2003

TECH CENTER 1600/2900

Day 1

' 1

Day 2

Day 4-6

Day 7



3 x 1.5 Gy

Tumor Processing

Figure 22

APR 0 2 2003 Docket No. TRANSMITTAL OF FORMAL DRAWINGS 02940139AA Schmidt-Ullrich, et al. In Re Application Of: Serial No. Filing Date Confirmation No. Examiner Art Unit 09/714,790 11/17/00 Chen 1632 GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND CARCINOMA CELL RADIOSENSIZATION Invention:

•

PE CROWN & TRADE

RECEIVED

APR 0 4 2003

TECH CENTER 1600/2900

MDA tumors, Ad transduction in vivo

MDA-EGFR-CD533 tumors

 $3 \times 1.5 \,\text{Gy}$

3 x 1.5 Gy

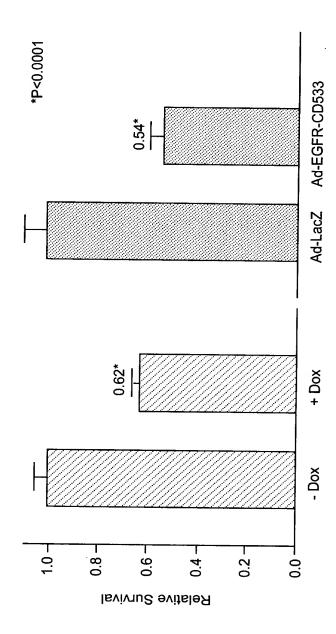
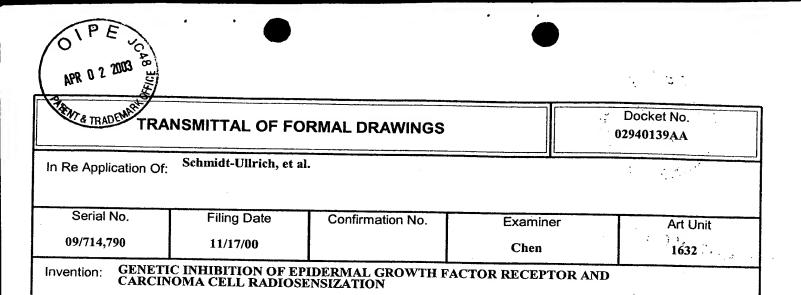


Figure 23





24/33

RECEIVE:

A-431 U-373 MG U-87 MG

TECHCENTER 1800:2900

ErbB-1

ErbB-2

Figure 24

APR 0 2 2003 &

INSMITTAL OF FORMAL DRAWINGS

Docket No. 02940139AA

In Re Application Of:

Schmidt-Ullrich, et al.

Serial No.

Filing Date

Confirmation No.

Examiner

Art Unit

09/714,790

11/17/00

Chen

1632

Invention:

GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND CARCINOMA CELL RADIOSENSIZATION

PATENT & TREET

RECEIVED

APR 0 4 2003

TECH CENTER 1600/2900

±0.4 ±0.3 ±0.1 ±0.2 U-373 MG Rad (2 Gy) ~ ပ ±0.1 ±0.3 ±0.2 ±0.7 ±0.2 ±0.3 1 1.1 2.3 1.4 3.0 2.8 2.5 2 5 10 Rad (2 Gy) U-87 MG Time (min) C Fold Change

Figure 25A

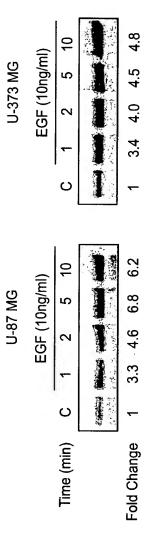
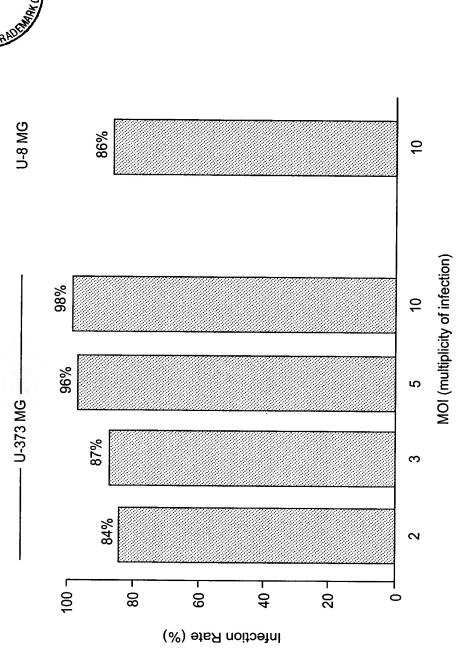


Figure 25B

APR 0 2 2003 Docket No. TRANSMITTAL OF FORMAL DRAWINGS 02940139AA Schmidt-Ullrich, et al. In Re Application Of: Serial No. Filing Date Confirmation No. Examiner Art Unit 09/714,790 11/17/00 Chen 1632 GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND CARCINOMA CELL RADIOSENSIZATION Invention:



PECEIVED APPROPRIED TO THE TO

Figure 26

APR 0 2 2003 Docket No. RANSMITTAL OF FORMAL DRAWINGS .02940139AA Schmidt-Ullrich, et al. In Re Application Of: Serial No. Filing Date Confirmation No. Examiner Art Unit 09/714,790 11/17/00 Chen 1632 GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND CARCINOMA CELL RADIOSENSIZATION

Invention:





		10	1	.8 3.4
LacZ	Gy)	5		6 .
J-87-AdLacZ	Rad (2 Gy)	2	1	2.3 1
⇒	Ľ	_	1	
	•	ပ	1	~
		Time (min)		Fold Change

		_	Rad (2 Gy)	: Gy)	
Time (min)	ပ	-	2	5	9
	1	1		8.	Ì
Fold Change	_	4.0	3.6	4.0 3.6 4.0 2.2	2.2

U-373-AdLacZ

533		9	1	0.9
-05	2 Gy)	5		1.
GFR	Rad (2 Gy)	2	7	6.0
U-87-EGFR-CD533		-	7	1.2
		ပ	4.5	-

533		10	1	1.0
R-CD	2 Gy)	5	6	0.9
-EGF	Rad (2 Gy)	7	0 1	1.0
U-373-EGFR-CD533		-	, 3	0.9
_		ပ	A. 7	_

Figure 27B

Figure 27A

APR 0 2 2003 Docket No. TRANSMITTAL OF FORMAL DRAWINGS 02940139AA Schmidt-Ullrich, et al. In Re Application Of: : Serial No. Filing Date Confirmation No. Examiner 09/714,790 11/17/00 Chen 1632 GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND CARCINOMA CELL RADIOSENSIZATION Invention:





Figure 28A



Figure 28B

Docket No. TRANSMITTAL OF FORMAL DRAWINGS 02940139AA Schmidt-Ullrich, et al. In Re Application Of: • Serial No. Filing Date Confirmation No. Examiner Art Unit 09/714,790 11/17/00 Chen 1632 GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND CARCINOMA CELL RADIOSENSIZATION Invention:



RECEIVED
APR 0 4 2003
TECH CENTER 1600/2900



Figure 29A

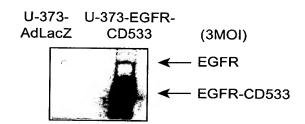


Figure 29B

Docket No. TRANSMITTAL OF FORMAL DRAWINGS 02940139AA Schmidt-Ullrich, et al. In Re Application Of: Filing Date Serial No. Confirmation No. Examiner Art Unit 09/714,790 11/17/00 Chen 1632

Invention:

GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND CARCINOMA CELL RADIOSENSIZATION

.

RECEIVED

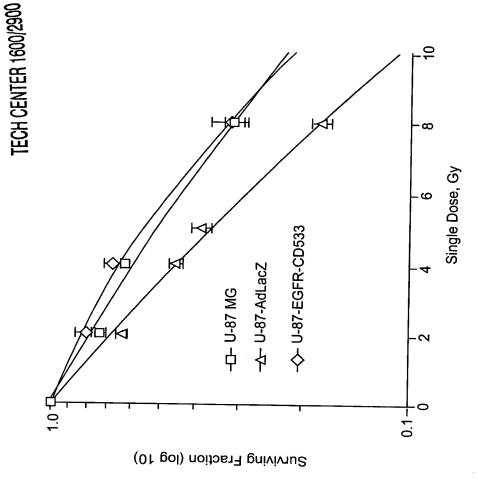


Figure 30

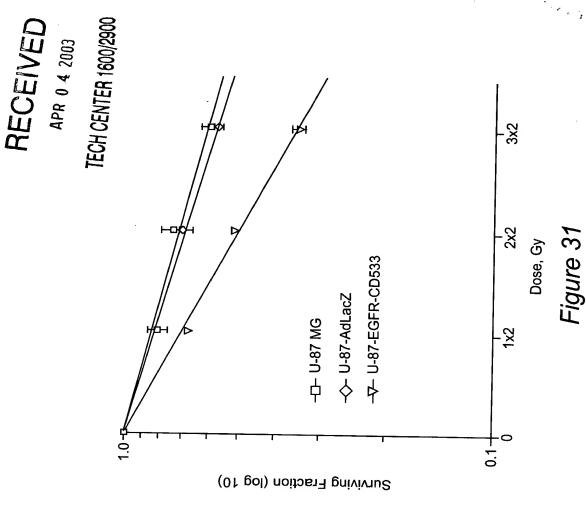
APR 0 2 2003 & Docket No. 02940139AA

In Re Application Of: Schmidt-Ullrich, et al.

Serial No. Filing Date Confirmation No. Examiner Art Unit 09/714,790 11/17/00 Chen 1632

Invention: GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR AND CARCINOMA CELL RADIOSENSIZATION





TRANSMITTAL OF FO			Docket No 02940139AA
APR 0 2 2003 Serial Ro.			
Serial 10. Serial 11/17/00	Confirmation No.	Examiner	Art Unit
		Chen	1632
Invention: GENETIC INHIBITION OF EL CARCINOMA CELL RADIOS	PIDERMAL GROWTH FAC ENSIZATION	CTOR RECEPTOR A	ND

•

RECEIVED

TECH CENTER 1600/2900

PE VCER

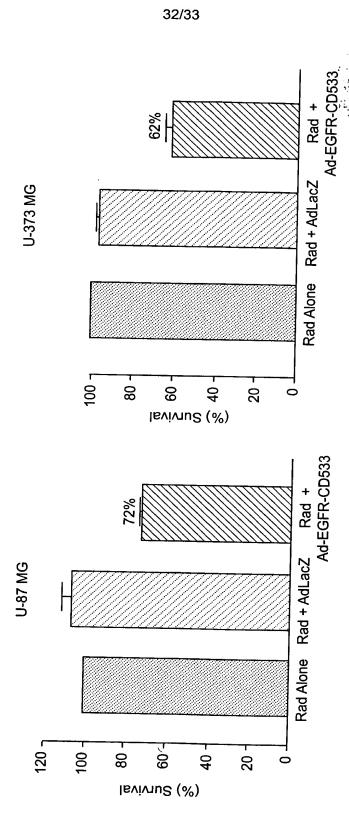


Figure 32

TRANSMITTAL OF FO			Docket No. 02940139AA
In Re Application Of: Schmidt-Ullrich, et a			
RADEMAN STORY	Confirmation No.	Examiner	Art Unit
11/17/00		Chen	1632
Invention: GENETIC INHIBITION OF EP CARCINOMA CELL RADIOSI	IDERMAL GROWTH FACENSIZATION	CTOR RECEPTOR AND	

•



AECEIVED

APROPAGO

TECHCENTER 1000/200

U-87 MG Tumor Xenografts

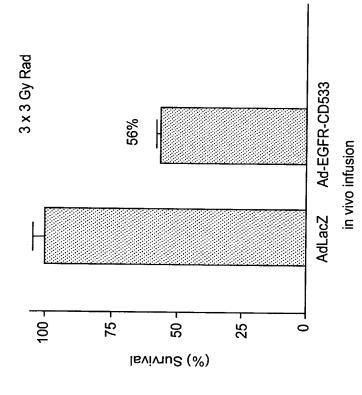


Figure 33

7 B

ж	n -	·	··· • ·	
		÷ 1.		• • • • • • • • • • • • • • • • • • •
TRANS	SMITTAL OF FO	DRMAL DRAWINGS		Docket No. 02940139AA
In Re Application Of: APR 0 2	أبيع	al.		
Serial No.	Fating Date	Confirmation No.	Examiner	Art Unit
09/714,790	11/17/00		Chen	1632
Invention: GENETIC CARCINO	INHIBITION OF E MA CELL RADIOS	PIDERMAL GROWTH F SENSIZATION	ACTOR RECEPTO	OR AND